REMARKS

Status of the Claims.

Claims 1-4, 7-8, 10-48, 62-66, 74-79, 93-94, 104-107, and 108-119 are pending with entry of this amendment. Claims 5-6, 9, 99, and 100 were previously cancelled without prejudice to subsequent renewal or filing in a continuation or divisional application. Claims 49-61, 67-73, 80-92, 95-98, and 101-103, which were withdrawn as being drawn to a nonelected invention(s), are canceled herein without prejudice to subsequent renewal. In addition, claims 13, 19, 20, 25, 29, 37-43, and 104 are canceled herein without prejudice to subsequent renewal. Applicants reserve the right to pursue claims relating to this canceled subject matter in subsequent applications and these claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action or as being made for any reason relating to patentability.

Claims 1-4, 7-8, 10, 12, 14, 17-18, 21-24, 26-28, 30-36, 46, 62, 65, 93-94, 105-107 are amended herein. These amendments to the pending claims introduce no new matter and are fully supported by the specification as filed. For example, claims 1, 4, 7-8, 10, 21-24, 26-28, 30-36, and 106 have been amended so as to be directed to the elected embodiments for which support is provided throughout the specification and the claims as originally filed. Claims 3, 8, 14, 17-20, and 105 have been amended to specify the control CMV promoter sequence of SEQ ID NO:19 or 20 used for comparison purposes. These sequences are provided in the specification including, e.g., in Figs. 8A-8I and p. 6, lines3-13. Support for the amendments to claim 3, which is dependent on claim 2, is provided in the specification, including at, but not limited to, e.g., originally filed claim 2 and Figures 8A-8I. Claim 4 has been amended for improved clarity. Claim 12 has been amended to correct an inadvertent typographical error. Support for the amendment to claim 8, which specifies a human CMV polynucleotide sequence shown in SEQ ID NO:19 or SEQ ID NO:20, is provided throughout the specification, including at, but not limited to, e.g., Figures 8A-8I. Claims 10, 21, 24, 26, 27, and 30-35 have been amended to correct an inadvertent typographical error. Specifically, the term "Figure 8" has been amended to specify more precisely Figures 8A-8I. Support for the amendment to claim 46 (which now specifies that the encoded polypeptide may be an enzyme) is provided in the specification, including at, but not limited to, e.g., page 64, line 26 to page 65, line 8.

New claims 108-119 have been added herein. These new claims introduce no new matter and support for the new claims is found generally throughout the specification. For example, support for new claim 108 is provided throughout the specification, including at, but not limited to,

e.g., originally filed claim 7. Support for new claim 110 is provided in the specification, including at, but not limited to, e.g., page 11, lines 1-5. Support for new claims 109 and 111, dependent on claim 108 and 110, respectively, is provided in the specification, including at, but not limited to, e.g., original claim 1. Support for new claim 112 is provided in the specification, including at, but not limited to, e.g., original claim 12.

Support for new claim 113 is provided in the specification, including at, but not limited to, e.g., original claims 62 and 63; page 63, lines 12-13; page 22, lines 24-29; and page 27, lines 22-28. Support for new claim 114, which is dependent on claim 113, is provided in the specification, including at, but not limited to, e.g., page 22, line 24 to page 23, line 2; page 7, lines 26-28. Support for new claims 115 and 116, each of which is dependent on claim 112, is provided in the specification, including at, but not limited to, e.g., page 7, lines 1-13 and Figure 9. Support for new claim 117 is provided in the specification, including at, but not limited to, e.g., original claims 62 and 63; page 63, lines 12-13; page 22, lines 24-29; page 27, lines 22-28; page 7, lines 1-13; and Figure 9. Support for new claims 118 and 119 is provided in the specification, including at, but not limited to, e.g., original claims 65 and 66.

The specification has been amended as indicated above to correct several inadvertent typographical errors. No new matter has been added by these amendments to the specification.

Information Disclosure Statement.

Applicants thank the Examiner for notifying them that copies of the cited references enclosed with the Information Disclosure Statement (IDS) mailed on November 6, 2001 had not been located. Applicants did receive confirmation by return postcard that the USPTO had received the IDS and references. Nevertheless, for the convenience of the Examiner, on January 15, 2003 Applicants filed a second copy of each reference cited on the IDS. Applicants respectfully request consideration of the references cited therein.

Claim Objections.

Claims 62-66 and 93-94 were objected to under 37 CFR 1.75(c) as being in improper form because a multiply dependent claim cannot depend from a multiply dependent claim. This objection has been rendered moot by the amendments to claims 62, 93, and 94.

Rejections Under 35 USC § 112.

Claims 1-4, 7-8, 10-48, and 74-79 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. In particular, the Examiner finds that each of these claims, with the exception of claim 38, is drawn to non-elected embodiments of the invention. Office Action, pp. 4-5. This rejection has been overcome by amending the claims to remove reference to non-elected embodiments. For example, independent claims 1, 10, and 106 have been amended to specify the polynucleotide sequence of SEQ ID NO:8. Dependent claims have been similarly amended for consistency.

Independent claims 1 and 106 were rejected as allegedly being vague and indefinite in that the metes and bounds of the phrase "or complementary sequence thereof" are unclear. Applicants have amended the claims as suggested by the Examiner to specify "the complementary sequence." Claims dependent upon claims 1 and 106 have been similarly amended for consistency.

Claims 2-3, 8, 14, 17-20, and 105 were rejected as allegedly being vague and indefinite because a specific human CMV promoter polynucleotide sequence for the comparison was not indicated. Applicants respectfully traverse this rejection. The phrase "a human CMV promoter polynucleotide sequence" is not vague or indefinite, since specific human CMV promoter polynucleotide sequences are known to those of skill in the art. However, in an effort to expedite prosecution, Applicants have amended claims 3, 8, 14, 17, 18, and 105 to specify more particularly the human CMV promoter polynucleotide sequence set forth in SEQ ID NO:19 or SEQ ID NO:20. The rejection has been mooted with regard to claim 2, since this claim has been amended to remove the phrase "a human CMV promoter polynucleotide sequence." The rejection has also been mooted with regard to claims 19-20, since these claims have been canceled. Withdrawal of the rejection is respectfully requested.

Claims 8, 14-16, 104, and 107 were rejected as allegedly being vague and indefinite because there was no clear and positive prior antecedent basis for the term "the polypeptide-encoding nucleic acid" in claim 1, upon which the rejected claims are dependent. Claims 8, 14, and 107 have been amended to specify "a polypeptide-encoding nucleic acid." With these amendments, Applicants believe the rejection of claims 8, 14, and 107, and claims 15-16, which are dependent on claim 14, has been overcome. The rejection has been mooted with regard to claim 104, as this claim has been canceled.

Rejections Under 35 USC § 102.

1. **A *Prima Facie* Case of Anticipation Based on Chapman Has Not Been Established for Any Rejected Claim.**

Claims 1-3, 4-8, 10-36, 44-48, 74-78, 104-105, and 107 were rejected under 35 USC § 102(b) as allegedly being anticipated by Chapman et al. (Nucleic Acids Research 19(14):3979-3986 (1991)) [hereinafter "Chapman"]. The Examiner states that Chapman teaches the construction and characterization of expression constructs comprising variations of a 2.4 kb fragment obtained for the hCMV Towne strain. The Examiner finds this 2.4 kb hCMV sequence has a 95.8% sequence identity to the polynucleotide sequence SEQ ID NO:8 and a local similarity of 98.8% over residues 335-2099 of the 2.4 kb sequence. The Examiner further finds that the fragments characterized by Chapman were shown to drive expression of different coding sequences used as reporters for promoter activity. Office Action, pp. 6-7.

Based on these findings, the Examiner takes the position that:

> Various of the rejected claims comprise limitations where the claimed nucleic acid drives expression of a reporter sequences at different levels relative to expression of the same reporter from a given reference CMV promoter. Given the levels of expression for the different constructs characterized by Chapman and given the high degree of identity to the constructs taught in the instant application, one of skill in the art would recognize that the constructs taught by Chapman would necessarily comprise the recited characteristics concerning expression levels in comparison to the reference CMV promoter. Similarly, one of skill in the art would recognize that the constructs of Chapman would express the encoding sequences well enough to induce an immune response in at least expression vectors. Because the Office does no have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or nonobvious difference between the claimed products and the products of the prior art (e.g., that the products of the prior art do not possess the same material structural and functional characteristics of the claimed products). See in re Best, 562 1252, 195 USPQ 430 (CCPA 1977).

Id.

Applicants respectfully traverse this rejection for at least the following reasons. First, Applicants note that claims 5-6, which were rejected as being anticipated by Chapman, were previously cancelled. Thus, this rejection does not properly apply to these claims. In addition, the

rejection has been mooted with respect to claims 13, 19-20, 25, 29 and 104, as these claims have been canceled herein.

Second, Applicants respectfully submit that a *prima facie* case of anticipation based on Chapman has not been established for any rejected claim. To establish a *prima facie* case of anticipation, it must be shown that each and every element as set forth in the claim is found in the cited prior art reference. Verdegaal Bros. V. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2s 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown as in complete detail as is contained in the . . . claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Of the rejected claims, only claims 1 and 10 are independent. These claims, and claims dependent thereon, are discussed below.

Claim 1

As presently amended, claim 1 specifies an isolated or recombinant nucleic acid comprising a polynucleotide sequence that has at least about 98% sequence identity to the polynucleotide sequence of SEQ ID NO:8 or the complementary polynucleotide sequence thereof. Applicants respectfully submit that the Office Action has not shown that Chapman teaches or suggests each and every element of claim 1. Specifically, it has not been shown that Chapman teaches or suggests ***an isolated or recombinant nucleic acid comprising a polynucleotide sequence that has at least about 98% sequence identity to that of SEQ ID NO:8***. Figure 1 of Chapman shows a specific polynucleotide sequence comprising a 2.361 kilobase segment of the 5' region of the major immediate-early gene of the human CMV (Towne). Notably, the Examiner concedes that the percent identity between the polynucleotide sequence of SEQ ID NO:8 and the 2.361 kilobase segment of the 5' end of the Towne human CMV IE gene is only 95.8%. Claim 1 specifies an isolated or recombinant nucleic acid comprising a sequence having at least about 98% identity to the polynucleotide sequence of SEQ ID NO:8. The 2.361-kb segment of the Towne hCMV IE gene disclosed in Chapman does not meet these limitations and thus does not anticipate the nucleic acid particularly defined by claim 1.

The Examiner states that an *arbitrary subsequence* of the disclosed 2.361-kb segment of the 5' end of the Towne hCMV IE gene, which subsequence comprises nucleotide residues 335-2099 of the 2.361-kb sequence, has a local similarity of 98.8% with the entire polynucleotide sequence of SEQ ID NO:8, which comprises 1767 nucleotide residues. Office Action, p. 6.

However, the fact that an arbitrary subsequence of the disclosed 2.361-kb 5' end segment of the Towne hCMV IE gene bears some sequence identity with Applicants' novel and useful chimeric promoter sequence is irrelevant and does not render the invention as specifically defined by claim 1 anticipated or obvious. Chapman does not teach or suggest any such subsequence comprising residues 335-2099 of the 2.361-kb segment. On the contrary, as shown below, Chapman explicitly ***teaches away*** from any fragment of the 2.361-kb segment of the Towne hCMV promoter IE gene that includes the first 400 base pairs of the gene, as this 400-bp region was found to have a negative impact on expression of a reporter coding sequence.

In particular, Chapman states that the 5' end of the Towne hCMV IE gene can be divided into 5 regulatory regions. *See* Chapman, p. 3981. The first approximately 400 base pairs contains a potential stem-loop structure and a cluster of four binding sites for nuclear factor 1 (NF1). *Id.* Chapman determined that:

> [W]hen the first 400 base pairs of the *Pst I* fragment were present in expression plasmids, poor expression of glycoproteins was observed in both monkey kidney cells (COS7) and in Chinese hamster ovary cells (DXB11). Deletion of these upstream modulatory sequences led to high levels of expression for several mammalian glycoproteins, suggesting a negative regulatory role for this region in the two cell types. Therefore, glycoprotein expression plasmids were constructed using both transcribed and untranscribed regulatory sequences, including intron A, but lacking 5' DNA containing the potential stem-loop structure and the first two NF1 binding sites (Fig. 3B).

Chapman, pp. 3982-83.

Thus, Chapman explicitly teaches that any fragment of the 2.361-kb segment of the 5' end of the Towne hCMV promoter IE gene cannot include the first 400 base pairs of the gene if it is to be functional. None of the 3 fragments that Chapman constructed and characterized included the potential stem-loop structure or the first two NF1 binding sites. In fact, none of the 3 fragments that Chapman characterized included the first 461 base pairs of the 2.361-kb segment of the Towne hCMV promoter IE gene. *See* Chapman, pp. 3981-3983, Fig. 3 and Table 1. Notably, the arbitrary subsequence that the Examiner points to, which comprises nucleotide residues 335-2099 of the gene (shown in the search report attached to Office Action, Result 9), contains a large portion of the 5' end region that Chapman finds to have a negative regulatory role, including the first two NF1 binding sites. That this arbitrary subsequence comprising residues 335-2099 of the 2.361-kb segment of the 5'end of the Towne hCMV IE gene bears some local similarity with the

polynucleotide sequence of SEQ ID NO:8 is irrelevant. Chapman does not teach or suggest any isolated or recombinant nucleic acid sequence comprising residues 355-2099 of the 2.361-kb segment of the 5'end of the Towne hCMV IE gene. Nor does Chapman teach or suggest that such a sequence comprising residues 355-2099 would possess any functional activity. Rather, Chapman effectively teaches that such a sequence would not function properly as a promoter.

The Examiner also contends that the three specific fragments of the 2.361-kb segment of the 5' end of the Towne hCMV IE gene that Chapman constructed have the same structural characteristics as the nucleic acid defined by claim 1 and would necessarily have the same functional characteristics concerning expression levels as recited in various rejected claims dependent upon claim 1. These arguments are without merit for at least the following reasons. None of the three Chapman fragments comprises a sequence that is at least 98% identical to the polynucleotide sequence of SEQ ID NO:8. Each fragment begins at nucleic acid residue 461 of the disclosed 2.361-kb segment of the Towne hCMV IE gene. Fragment B, which includes a promoter/enhancer region and intron A, is a 1636 bp fragment comprising nucleotides 461-2097 (see Chapman's Fig. 3B, Table I, and p. 3980). Fragment C, which begins with nucleotide 461, includes the promoter/enhancer region, but does not include intron A (see Chapman's Fig. 3C and p. 3980). Fragment D, which also begins with nucleotide 461 of the disclosed 2.361-kb segment of the Towne hCMV IE gene, comprises the promoter/enhancer region and a mutant intron A domain (see Chapman's Fig. 3D, p. 3980). Significantly, as discussed above, none of these fragments includes any nucleotide residues within the first 400 bases of the 5'end of the 2.361 segment of the Towne hCMV IE gene. In contrast, the polynucleotide sequence of SEQ ID NO:8 includes an additional 127 nucleotide residues at the 5' end that are not found in any of the three Chapman fragments. Compare, for example, the polynucleotide sequence of SEQ ID NO:8 with the subsequence comprising nucleotides 335-2099 of the 2.361-kb segment of the Towne hCMV IE gene, as shown in the alignment of the search report attached to Office Action, Result 9. In this alignment, the first residue of each of the three Chapman fragments is at nucleotide residue 461, which corresponds to nucleotide 127 of SEQ ID NO:8. Thus, the nucleic acid sequences of the three fragments disclosed in Chapman differ dramatically in structure from the nucleic acid defined by claim 1. Furthermore, the 5' end of the polynucleotide sequence of SEQ ID NO:8 includes regions that share sequence identity with the first two NF1 factors -- the factors that are *expressly excluded* from all of the Chapman fragments. Given Chapman's teaching that the presence of such NF1 factors in expression

plasmids have a negative effect on the expression of an operably liked reporter gene, one of skill would not have concluded that the nucleic acid sequence of claim 1 would have the same or substantially the same functional characteristics as any of the promoter sequence fragments taught by Chapman.

Moreover, the facts of *In re Best* do not support the Examiner's conclusion. In that case, the prior art reference disclosed aluminosilicate compositions comprising SiO_2/Al_2O_3 and Na_2O/Al_2O_3 compounds *identical in structure and molar ratios* to those claimed. Given that the prior art reference disclosed compounds that were structurally identical to those claimed, the court reasoned that the applicant had the burden to show a novel or unobvious difference between his claimed compounds and the prior art compounds. *See In re Best*, 195 USPQ 430, 434 (1977). That case is immaterial to the instant application, since the nucleic acid sequences taught by Chapman are not structurally identical to those claimed by Applicants.

For at least these reasons, Applicants submit that the Office Action has not established a *prima facie* case of anticipation based of Chapman. It has not been shown that Chapman taught or suggested each and every element of claim 1, or claims2-4, 7-8, 12, 14-18, 21-24, 26-28, 30-36, 44-48, 74-78, and 107 dependent thereon. Applicants submit that the rejection is improper and respectfully requested that it be withdrawn.

Claim 10

Claim 10 is directed to an isolated or recombinant nucleic acid comprising a ***subsequence of the polynucleotide sequence of SEQ ID NO:8***, said subsequence comprising nucleic acid residues at positions of the polynucleotide sequence of SEQ ID NO:8 ***corresponding to position 1 to about position 909*** of the consensus sequence shown in Figures 8A-8I, or the complementary polynucleotide sequence thereof (emphasis added).

Here, too, the Office Action has failed to show that Chapman discloses each and every limitation of claim 10. None of the three specific fragments of the 2.361-kb segment of the Towne hCMV IE gene taught by Chapman comprises a sequence identical to the claimed nucleic acid comprising nucleotide residues 1-909 of SEQ ID NO:8. Nor is there any suggestion that any of the 3 Chapman fragments would have the same functional characteristics concerning expression levels as recited in any rejected claim dependent upon claim 10. On the contrary, as noted above, each Chapman fragment explicitly *excludes* a region comprising the first 400 bases of the 5'end of

the 2.361-kb segment of the Towne hCMV IE gene, because such region contained NF1 binding sites that negatively affected expression of an operably linked heterologous gene.

As shown above, the nucleic acid defined by claim 10 includes an additional 127 nucleotide residues at its 5' end that are not included in any of the Chapman fragments. Thus, the nucleotide sequences of the three Chapman fragments differ dramatically in structure from the nucleic acid of claim 10. Furthermore, the nucleic acid of claim 10 comprises a polynucleotide sequence that includes regions that are identical with the first two NF1 factors of the hCMV Towne gene. Chapman teaches that the presence of such NF1 factors in expression plasmids have a negative effect on the expression of an operably liked reporter gene. Consequently, one of skill would not have concluded that the nucleic acid sequence of claim 1 would have the same or substantially the same functional characteristics as any of the fragments taught by Chapman.

For at least these reasons, Applicants submit that the Office Action has not established a *prima facie* case of anticipation based. It has not been shown that Chapman teaches or suggests every element of claim 10 or claims 11, 44-48 74-78, and 105 dependent thereon. Withdrawal of the rejection is respectfully requested.

2. **A *Prima Facie* Case of Anticipation Based on Bebbington Has Not Been Established for Any Rejected Claim.**

Claims 1-3, 4-8, 10-36, 44-48, 74-78, 104-105, and 107 were rejected under 35 USC § 102(b) as allegedly being anticipated by Bebbington (WO 89-01036A1 or WO 89/01036A2) [hereinafter "Bebbington"]. The Examiner states that Bebbington teaches the construction and use of expression vectors comprising the complete 5'-untranslated region including the first introns of the major immediate early gene of human CMV. The Examiner finds that the sequences taught by Bebbington comprise 95.9% sequence identity to SEQ ID NO:8. Further, the Examiner finds that local similarity over about 1.77 kb of the Bebbington promoter sequence reaches levels of up to 97.8% identity with the entire sequence of SEQ ID NO:8. The Examiner takes the position that "[v]arious of the rejected claims comprise limitations where the claimed nucleic acid drives expression of a reporter sequences at different levels relative to expression of the same reporter from a given reference CMV promoter. Given the levels of expression for the different constructs characterized by Chapman and given the high degree of identity to the constructs taught in the instant application, one of skill in the art would recognize that the constructs taught by Chapman

would necessarily comprise the recited characteristics concerning expression levels in comparison to the reference CMV promoter. Similarly, one of skill in the art would recognize that the constructs of Chapman would express the encoding sequences well enough to induce an immune response in at least expression vectors." Office Action, p. 8. The Examiner concludes that Applicants have the burden to show a novel or nonobvious difference between the claimed products and the products of the prior art.

Applicants respectfully traverse this rejection for at least the following reasons. First, claims 5-6 were previously cancelled and claims 13, 19-20, 25, 29 and 104 have been canceled herein. Thus, this rejection does not apply to these claims and should be withdrawn. Second, as discussed in detail below, Applicants respectfully submit that a *prima facie* case of anticipation based on Bebbington has not been established for any rejected claim.

Claim 1

Applicants respectfully submit the Office Action has not shown that Bebbington teaches or suggests each and every element of claim 1. Claim 1 specifies an isolated or recombinant nucleic acid comprising a polynucleotide sequence that has at least about 98% sequence identity to the polynucleotide sequence of SEQ ID NO:8 or the complementary polynucleotide sequence thereof. No sequence disclosed or suggested in Bebbington meets all of these limitations. The Examiner points out that Bebbington discloses a human CMV promoter sequence having about 95.9% sequence identity to the sequence of SEQ ID NO:8. Clearly, though, that sequence does not serve to anticipate claim 1, since it is not at least about 98% identical to the polypeptide sequence of SEQ ID NO:8. Significantly, the polynucleotide sequence disclosed by Bebbington comprises 2129 nucleotide residues. The sequence set forth in SEQ ID NO:8 is 1676 nucleotide residues in length. The fact that a local similarity over about 1.77 kb of the Bebbington promoter sequence reaches levels of up to 97.8% identity with the entire sequence of SEQ ID NO:8 is of no consequence. Bebbington does not teach or suggest any specific fragment of the disclosed 2129-nucleotide sequence comprising only 1676 residues. On the contrary, Bebbington expressly states that the present invention is based on the discovery that vectors containing a DNA sequence comprising the promoter, enhancer and *complete or at least substantially complete* 5'-untranslated region of the major immediate early gene of the human CMV upstream of a heterologous gene result in high expression of the heterologous gene product. *See, e.g.*, Bebbington, p. 3, lines 13-28. Nor does Bebbington teach or suggest that such a fragment would have any function -- let alone be capable of

serving as a promoter. The Bebbington nucleic acid differs dramatically in structure from Applicants' nucleic acid defined by claim 1.

For at least these reasons, Applicants submit that the Office Action has not shown that Chapman teaches or suggests each and every element of claim 1 or claims 2-4, 7-8, 12, 14-18, 21-24, 26-28, 30-36, 44-48, 74-78, and 107 dependent thereon. The rejection is thus improper and its withdrawal is respectfully requested.

Claim 10

The Office Action has also not shown that Bebbington teaches or suggests each and every element of claim 10. Claim 10 specifies an isolated or recombinant nucleic acid comprising a subsequence of the polynucleotide sequence of SEQ ID NO:8 that comprising nucleic acid residues at positions of the sequence of SEQ ID NO:8 corresponding to positions 1 to about 909 of the consensus sequence shown in Figures 8A-8I, or the complementary polynucleotide sequence thereof.

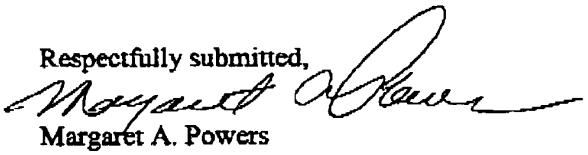
Bebbington discloses a particular human CMV promoter sequence that is 2129 nucleotide residues in length. Bebbington does not teach or suggest any specific fragment of the disclosed 2129-nucleotide sequence comprising only about 909 residues. Nor does Bebbington teach or suggest that such a fragment would have any function -- let alone be capable of serving as a promoter. Rather, Bebbington expressly states that the functional sequence comprises the promoter, enhancer and *complete or at least substantially complete* 5'-untranslated region of the major immediate early gene of the human CMV. *See, e.g.*, Bebbington, p. 3, lines 13-28. Thus, the Bebbington nucleic acid and Applicants' nucleic acid as defined by claim 10 differ dramatically in structure.

Because it has not been shown that each and every element of claim 1 is disclosed in Bebbington, a *prima facie* case of anticipation has not been made. For at least these reasons, Applicants submit that the rejection of claim 10, and claims 11, 44-48 74-78, and 105 dependent thereon, is improper and request that it be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application in any way, the Examiner is invited to telephone the undersigned at (650) 298-5809.

Respectfully submitted,



Margaret A. Powers
Attorney for Applicants
Reg. No. 39,804

Maxygen, Inc.
Intellectual Property Department
515 Galveston Drive
Redwood City, CA 95063
Telephone: 650-298-5300
Facsimile: 650-298-5446
Customer No.: 30560